CANCER FACTS
National Cancer Institute • National Institutes of Health

Gene for Kidney Cancer Isolated

A research team headed by scientists at the National Cancer Institute (NCI) identified the gene responsible for the most common type of kidney cancer, and reported on their work in the May 1994 issue of *Nature Genetics*.* This cancer, called sporadic (nonfamilial) clear cell carcinoma, accounts for about 23,500 newly diagnosed cases of kidney cancer each year, or about 85 percent of all cases of the disease.

"With identification of this kidney cancer gene, it may be possible to develop new methods to improve the diagnosis and treatment of the disease and potentially to find ways to prevent it," said W. Marston Linehan, M.D., of NCI's Surgery Branch. "The finding also may make it possible to develop a blood or urine test that can detect kidney cancer early when it is most treatable."

The damaged or mutated gene responsible for sporadic clear cell carcinoma of the kidney is a tumor suppressor gene located on the short arm of chromosome 3. The protein produced by the gene appears to normally restrain growth. The researchers found that this gene is mutated (inactivated) in a high percentage of tumors or cell lines (57 percent) from patients with sporadic, nonfamilial kidney cancer.

* Gnarra JR, Tory K, Weng Y, et al. "Mutations of the VHL tumor suppressor gene in renal carcinoma," *Nature Genetics* 1994; 7(1):85–90.

"The disease appears to fit the two-hit model for development of cancer, where both copies of the critical gene are damaged or mutated," said co-investigator Berton Zbar, M.D., Chief of NCI's Laboratory of Immunobiology. (There are two copies of every gene in most cells. One normal copy of a gene is sufficient to prevent development of cancer. If both copies are damaged or mutated—the two-hit model—cancer may develop.)

The researchers also found that the kidney cancer gene is affected early in the development of the disease. This finding is important, Dr. Linehan explained, because its early presence makes it possible to consider development of treatments to halt or reverse the progression of disease in its early stages.

The gene responsible for sporadic clear cell carcinoma is the same gene that was identified last year as the cause of the inherited cancer syndrome called von Hippel-Lindau (VHL) disease.** This research on clear cell carcinoma of the kidney was conducted by Michael I. Lerman, M.D., Ph.D., of NCI's Laboratory of Immunobiology, and Dr. Zbar, in collaboration with Dr. Linehan and colleagues. People who have VHL disease are predisposed to develop multiple tumors, including cancers of the kidney, eye, brain, spinal cord, and adrenal gland. Isolation of the VHL gene is now leading to improved identification of carriers of the gene in affected families to better manage the disease.

After the initial discovery of the VHL gene, these scientists, in collaboration with Richard D. Klausner, M.D., Director of the NCI, and his laboratory, initiated intensive studies of the gene's function. These studies have lead to the development of potential new forms of therapy for kidney cancer and VHL, which will be evaluated at the NCI and elsewhere.

**Latif F, Tory K, Gnarra J, et al. "Identification of the von Hippel-Lindau disease tumor suppressor gene," *Science* 1994; 260:1317–1320.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://www.cancer.gov to reach NCI's Web site.

CancerMail Service

To obtain a contents list, send e-mail to cancermail@icicc.nci.nih.gov with the word "help" in the body of the message.

CancerFax® fax on demand service

Dial 301–402–5874 and listen to recorded instructions.

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